

Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

This submission is accompanied by a Request for Continued Examination, a petition for extension of time, and an information disclosure statement. Because the Notice of Appeal was entered on June 18, 2007, this submission is timely. All fees should be withdrawn from Deposit Account 14-1138.

Claim 1 has been amended to recite higher stringency requirements (i.e., structural requirements of the claimed DNA molecule based on hybridization capability) as well as the presence of delta and tau subunits, with which the delta prime subunit form the clamp loader complex. The latter limitation finds descriptive support in the background of the invention at page 2, line 18 to page 3, line 31.

Claims 9 and 10 have been cancelled.

Claims 1, 2, 5, 7, 8, and 11-19 are pending. Claims 16-19 stand allowed.

The rejection of claims 1, 2, 5, and 7-15 under 35 U.S.C. §112 (first paragraph) for lack of written descriptive support is respectfully traversed.

The U.S. Patent and Trademark Office (“PTO”) maintains its position that the single species disclosed as SEQ ID NO: 148 (*Thermotoga maritima* delta prime subunit), and clamp loader complexes formed therewith, does not provide descriptive support for the genus of clamp loader complexes as claimed. Applicants respectfully disagree.

Given the recitation of high stringency conditions in claim 1 (hybridization and wash conditions of 5X sodium citrate buffer and at a temperature of 65°C), persons of skill in the art would expect hybridizing nucleic acids to be structurally similar to the nucleic acid sequence of SEQ ID NO: 147, and that the encoded proteins would be structurally and functionally similar to the delta prime subunit of SEQ ID NO: 148. *See EnzoBiochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1327, 63 USPQ2d 1609, 1615 (citing U.S. Patent and Trademark Office “Synopsis of Application of Written Description Guidelines” with approval). Given this rational expectation, persons of skill in the art would also expect related organisms (i.e., from bacterial genus *Thermotoga*) to share functional and structural similarities, including similarities in the structure and function of individual genes and their encoded proteins.

The reasonableness of that expectation is confirmed by attached Exhibits 1-3. Exhibit 1 is a copy of Genbank Accession CP000702 for *Thermotoga petrophila* RKU-1, which lists the nucleotide and amino acid sequences for a DNA polymerase III subunit designated as “gamma/tau subunits-like.” This was identified by BLAST search of the *Thermotoga petrophila* genome using the *Thermotoga maritima* delta prime subunit of SEQ ID NO: 148. A ClustalW amino acid alignment between the *Thermotoga maritima* delta prime subunit of SEQ ID NO: 148 with the *Thermotoga petrophila* delta prime subunit is shown in Exhibit 2 (approximately 95% identity), and an Emboss Align nucleotide alignment between *Thermotoga maritima* *holB* of SEQ ID NO: 147 with the *Thermotoga petrophila* *holB* is shown in Exhibit 3 (approximately 95% identity). Both of these alignments were performed by the undersigned attorney using the default settings of the software available from the European Bioinformatics Institute website.

Given the above facts, applicants respectfully submit that the present application provides written descriptive support for the claimed subject matter. Therefore, the rejection of claims 1, 2, 5, and 7-15 for lack of written description should be withdrawn.

The rejection of claims 1, 2, 5, and 7-15 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making other delta prime subunits and using those subunits to form clamp loader complexes within the scope of the claims. Applicants respectfully disagree.

Because the application adequately describes the presently claimed genus, persons of skill in the art would be fully able to obtain other polynucleotides encoding other delta prime subunits encompassed by the hybridization limitations recited in claim 1, express and recover the encoded delta prime subunits, and allow recovered delta prime subunits to assemble with delta and tau subunits into a clamp loader complex.

The present application provides the nucleotide sequence of *Thermotoga maritima* *holB* (SEQ ID NO: 147) and the encoded delta prime subunit (SEQ ID NO: 148). The present application further describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42, line 29; *see also* Example 20 regarding isolation of *A. aeolicus* *holB*), express the delta prime subunit encoded by such homologous *holB* sequences (*see* Example 20 regarding expression of *A. aeolicus* delta prime), and test the encoded delta subunit for clamp loader assembly competence (*see* Examples 24 and 25 regarding

assembly of *A. aeolicus* clamp loader) and for clamp loader activity (*see* Examples 26 and 30 regarding activity of *A. aeolicus* clamp loader). Thus, one of ordinary skill in the art would have been fully able to make and use proteins and clamp loader complexes within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the delta prime homolog shown in Exhibit 1 (attached hereto). For this reason, it should be apparent that the present application fully enables the production and use of other species of *Thermotoga holB* homologs and their encoded delta prime subunits.

For these reasons, applicants submit that the rejection of claims 1, 2, 5, and 7-15 for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: January 18, 2008

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Exhibit 1: Genbank Accession CP000702



PubMed

Nucleotide

Protein

Genome



Structure

PMC

Taxonomy

OMIM

My NCBI

[Sign In] [Register]

Books

Search Nucleotide

for

Go

Clear

Limits

Preview/Index

History

Clipboard

Details

Display GenBank(Full)

Show 5

Send to

Hide:

☐ sequence☐

all but gene, CDS and mRNA features

Range: from 148657

to 149595

Show whole sequence

☐ Reverse complemented strand

Features: [

1: CP000702. Reports *Thermotoga petrophila* petrop...[gi:147734689]

Links

Comment Features Sequence

LOCUS CP000702 939 bp DNA linear BCT 06-DEC-2007

DEFINITION *Thermotoga petrophila* RKU-1, complete genome.

ACCESSION CP000702 REGION: 148657..149595

VERSION CP000702.1 GI:147734689

PROJECT GenomeProject:17089

KEYWORDS .

SOURCE *Thermotoga petrophila* RKU-1

ORGANISM *Thermotoga petrophila* RKU-1

Bacteria; Thermotogae; Thermotogales; Thermotogaceae; *Thermotoga*.

REFERENCE 1 (bases 1 to 939)

AUTHORS Copeland,A., Lucas,S., Lapidus,A., Barry,K., Glavina del Rio,T., Dalin,E., Tice,H., Pitluck,S., Sims,D., Brettin,T., Bruce,D., Detter,J.C., Han,C., Tapia,R., Schmutz,J., Larimer,F., Land,M., Hauser,L., Kyrpides,N., Mikhailova,N., Nelson,K., Gogarten,J.P., Noll,K. and Richardson,P.

TITLE Complete sequence of *Thermotoga petrophila* RKU-1

JOURNAL Unpublished

REFERENCE 2 (bases 1 to 939)

AUTHORS Copeland,A., Lucas,S., Lapidus,A., Barry,K., Glavina del Rio,T., Dalin,E., Tice,H., Pitluck,S., Sims,D., Brettin,T., Bruce,D., Detter,J.C., Han,C., Tapia,R., Schmutz,J., Larimer,F., Land,M., Hauser,L., Kyrpides,N., Mikhailova,N., Nelson,K., Gogarten,J.P., Noll,K. and Richardson,P.

TITLE Direct Submission

JOURNAL Submitted (14-MAY-2007) US DOE Joint Genome Institute, 2800 Mitchell Drive B100, Walnut Creek, CA 94598-1698, USA

COMMENT URL -- <http://www.jgi.doe.gov>

JGI Project ID: 4002277

Source DNA and bacteria available from Kenneth Noll (kenneth.noll@uconn.edu)

Contacts: Kenneth Noll (kenneth.noll@uconn.edu)

Paul Richardson (microbes@cuba.jgi-psf.org)

Quality assurance done by JGI-Stanford

Annotation done by JGI-ORNL and JGI-PGF

Finishing done by JGI-LANL

Finished microbial genomes have been curated to close all gaps with greater than 98% coverage of at least two independent clones. Each base pair has a minimum q (quality) value of 30 and the total error rate is less than one per 50000.

The JGI and collaborators endorse the principles for the distribution and use of large scale sequencing data adopted by the larger genome sequencing community and urge users of this data to follow them. It is our intention to publish the work of this project in a timely fashion and we welcome collaborative interaction on the project and analysis.

(<http://www.genome.gov/page.cfm?pageID=10506376>).

FEATURES Location/Qualifiers

source 1..939
/organism="Thermotoga petrophila RKU-1"
/mol_type="genomic DNA"
/strain="RKU-1"
/db_xref="taxon:390874"
gene complement(<1..10)
/locus_tag="Tpet_0156"
CDS complement(<1..10)
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/note="PFAM: PSP1 domain protein"
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GLGLCGLPTCCSTFLRDFSSVTLKHAKKQQMMINPAKISGPCRRLLCCLTYEYDFYEK
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CDS complement(1..939)
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/transl_table=11
/product="DNA polymerase III gamma/tau subunits-like
protein"
/protein_id="ABQ46186.1"
/db_xref="GI:147734846"
/translation="MNDLIRKYAKDQLEILKRIIEKSEGISILINGEDLSYPREVSLE
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QQAANAFKLTLEEPPEYAVIVLNTRHWHYLLPTIKSRVFRVVNVPKFRDLVKEKIG
DFWEELPLLERDFKTAPEAYKLGAELSGLMESLKVLETEKLLKKALSEGLEGYLACR
ELLERFSKVESKEFFALFDQLTNTITGKDSFLLIQRLTRIVLHENTWESVEDQKSVSF
LDSILRVKIANLNNKLTLMNILAIHREKRKGVNAWS"

ORIGIN

```
1  tcagctccaa  gcgttgacac  ctctctttct  ctctctgtgt  atcgcgagaa  tattcateag
61  agtgagtttg  ttgttcagat  tcgtatattt  caccctgaga  attgaatcga  ggaaagacac
121  gcttttttga  tcttcaacgc  tttcccaggt  gttttcgtga  aggacaattc  ttgtcagttc
181  ctggatcaaa  agaaatgagt  cttttcccg  tatcgtgttg  gttaattggt  caaaaagcgc
241  aaagaattcc  ttcgattcca  cttttgaaa  tctctccaga  agctccctac  acgcgagata
301  accctcgagt  cttctgaaa  gggctttctt  taagagtttt  tccgtctcca  aaactttgag
361  actttccatc  aatccagaaa  gtttttcgc  accaagtttg  taggcttcga  aagccgtttt
421  gaagtctctc  tcaaggagcg  gaagtctctc  ccagaaatcg  cctattttct  ctttcacgag
481  atctctgaac  tcttttgga  cgttcacaac  cactctgaac  actcggctct  ttatcgtcgg
541  cagtagataa  tgcagtggt  ggggtgtcag  aacgatacaca  gcgtattctg  gcggttcttc
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841  ttctccgttt  atgagaatgg  atattccttc  agactttct  atgatccttt  tcaaaatttc
901  cagttgatct  ttagegtact  ttctgatcaa  atcgttcat
```

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NCBI | NLM | NIH

Aug 28 2007 16:53:42

Exhibit 2: ClustalW (Amino Acid) Alignment

CLUSTAL W 2.0 multiple sequence alignment

Sequence format is Pearson
number of seqs is: 2
Sequence 1: SEQ147 311 aa
Sequence 2: T_petrophila 312 aa

comparing
paramArg[setSeqNoRange]= off
comparing

Start of Pairwise alignments

Sequences (1:2) Aligned. Score: 95
Guide tree file created: [/ebi/extserv/clustalw-
work/interactive/2007122119/clustalw2-20071221-19204050.dnd]

CLUSTAL-Alignment file created [/ebi/extserv/clustalw-
work/interactive/2007122119/clustalw2-20071221-19204050.aln]

```
SEQ148      MNDLIRKYAKDQLETLKRIIEKSEGISILINGEDLSYPREVSLELPEYVEKFPPKASDVL 60
T_petrophila MNDLIRKYAKDQLEILKRIIEKSEGISILINGEDLSYPREVSLELPEYVEKFPPKASDVL 60
*****

SEQ148      EIDPEGENIGIDDIRTIKDFLNYSPELYTRKYVIVHDCERMTQQAANAFKALEEPPEYA 120
T_petrophila EVDPEEENIGIDEIRTIKDFLNYSPELYTRKYVIVHDCERMTQQAANAFKLTLEEPPEYA 120
*:*:* *****;*****;*****;*****;*****

SEQ148      VIVLNTRRWHYLLPTIKSRVFRVVVNPKEFRDLVKEKIGDLWEELPLLERDFKTALEAY 180
T_petrophila VIVLNTRHWHYLLPTIKSRVFRVVVNPKEFRDLVKEKIGDFWEELPLLERDFKTALEAY 180
*****;*****;*****;*****;*****;*****;*****

SEQ148      KLGAEKLSGLMESLKVLETEKLLKKVLSKGLEGYLACRELLERFSKVESKEFFALFDQVT 240
T_petrophila KLGAEKLSGLMESLKVLETEKLLKALSEGLEGYLACRELLERFSKVESKEFFALFDQLT 240
*****;*****;*****;*****;*****;*****;*****

SEQ148      NTITGKDAFLLIQRLTRIILHENTWESVED-KSVSFLDSILRVKIANLNNKLTLMNILAI 299
T_petrophila NTITGKDSFLLIQRLTRIVLHENTWESVEDQKSVSFLDSILRVKIANLNNKLTLMNILAI 300
*****;*****;*****;*****;*****;*****;*****

SEQ148      HRERKRGVNAWS 311
T_petrophila HRERKRGVNAWS 312
*****
```


Exhibit 3: Emboss Align (Nucleic Acid) Alignment

```
#####
# Program: needle
# Rundate: Fri Dec 21 19:40:04 2007
# Align_format: srspair
# Report_file: /ebi/extserv/old-work/needle-20071221-19400372876934.output
#####
```

```
#=====
#
# Aligned_sequences: 2
# 1: SEQ147
# 2: T_petrophila
# Matrix: EBLOSUM62
# Gap_penalty: 10.0
# Extend_penalty: 0.5
#
# Length: 939
# Identity: 890/939 (94.8%)
# Similarity: 890/939 (94.8%)
# Gaps: 3/939 ( 0.3%)
# Score: 5073.0
#
#
#=====
```

SEQ147	1	atgaacgatttgatcagaaagtacgctaaagatcaactggaaactttgaa	50
T_petrophila	1	atgaacgatttgatcagaaagtacgctaaagatcaactggaaattttgaa	50
SEQ147	51	aaggatcatagaaaagtctgaaggaatatccatcctcataaatggagaag	100
T_petrophila	51	aaggatcatagaaaagtctgaaggaatatccattctcataaacggagaag	100
SEQ147	101	atctctcgatccgagagaagtatcccttgaacttcccgagtacgtggag	150
T_petrophila	101	atctctcgatccgagagaagtatcccttgaacttcccgagtacgtggag	150
SEQ147	151	aaatttcccccgaggcctcggtgttctggagatagatcccgaggggga	200
T_petrophila	151	aaatttcccccgaggcctcggtgttctggaggtagatcccgaggagga	200
SEQ147	201	gaacataggcatagacgacatcagaacgataaaggacttctgaactaca	250
T_petrophila	201	gaacataggatagacgaaatcagaacgataaaggacttctgaactaca	250
SEQ147	251	gccccgagctctacacgagaaagtacgtgatagtcacgactgtgaaaga	300
T_petrophila	251	gccctgaactctacacgagaaagtacgtgatagtcacgactgtgaaaga	300
SEQ147	301	atgaccagcaggcgggcgaacgcgtttctgaaggcccttgaagaaccaac	350
T_petrophila	301	atgaccagcaggcgggcgaacgcgtttctgaaaacccttgaagaaccgcc	350
SEQ147	351	agaatacgtgtgatcggttctgaacactcgccgctggcattatctactgc	400
T_petrophila	351	agaatacgtgtgatcggttctgaacacccgccactggcattatctactgc	400

SEQ147	401	cgacgataaaagagccgagtggttcagagtggttggaacgttccaaaggag	450
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SEQ147	451	ttcagagatctcgtgaaagagaaaataggagatctctgggaggaacttcc	500
T_petrophila	451	ttcagagatctcgtgaaagagaaaataggcgatttctgggaggaacttcc	500
SEQ147	501	acttcttgagagagacttcaaaacggctctcgaagcctacaaacttggtg	550
T_petrophila	501	gctccttgagagagacttcaaaacggcttctcgaagcctacaaacttggtg	550
SEQ147	551	cggaaaaaactttctggattgatggaaagtctcaaagttttggagacggaa	600
T_petrophila	551	cggaaaaaactttctggattgatggaaagtctcaaagttttggagacggaa	600
SEQ147	601	aaactcttgaaaaaggctcctttcaaaaggcctcgaagggttatctcgcatg	650
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SEQ147	651	tagggagctcctggagagattttcaaagggtggaatcgaaggaattctttg	700
T_petrophila	651	tagggagcttctggagagattttcaaagggtggaatcgaaggaattctttg	700
SEQ147	701	cgttttttgatcaggtgactaacacgataacaggaaaagacgcgtttctt	750
T_petrophila	701	cgttttttgaccaattaaccaacacgataacgggaaaagactcatttctt	750
SEQ147	751	ttgatccagagactgacaagaatcatttccacgaaaacacatgggaaag	800
T_petrophila	751	ttgatccagagactgacaagaattgtccttcacgaaaacacctgggaaag	800
SEQ147	801	cgttgaagatcaaaaaagcgtgtctttcctcgattcaattctcaggggtga	850
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SEQ147	901	cacagagagagaaagagaggtgtcaacgccttgagc	936
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